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Study to Assess Rational Use of Antifungal Medications at a Clinic in Mbabane, Eswatini

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Abstract: Inappropriate use of antifungal agents is implicated in the development of antifungal resistance and can lead to adverse outcomes like persistent infections, unnecessary exposure and increased cost. Rational drug use can be assessed using World Health Organization / International Network of Rational Use of Drugs core drug use indicators as they are reliable in measuring aspects of health provider behavior in primary healthcare facilities. This was a quantitative research approach using a descriptive, retrospective cross-sectional design conducted to assess the rational use of antifungal medications, completeness of prescriptions and antifungal prescribing patterns at a clinic in Mbabane, Eswatini. The study covered the patient's electronic data for a period of one year (1st January 2018- 31st December 2018) and patients receiving antifungal medications in July 2019. A total of 168 antifungal prescriptions were selected and used by random sampling method, 30 patients and 1 Pharmacy personnel were randomly sampled for a prospective review. Percentages were reported for categorical variables while the mean and standard deviation were used to summarize the data for continuous variables. The majority of patients to whom these drugs were prescribed were diagnosed to have tinea corporis (57.74%) followed by oral candidiasis (15.48%). Benzoic acid was the most commonly prescribed antifungal drug (27.98%) followed by griseofulvin (16.07%). With regards to prescribing indicators the average drugs per encounter was 3.30, percent medicines prescribed by generic name was 87.77%, percent encounters with an antibiotic were 6.24%, percent encounter with an injection was 0.45% and medicines from the Essential Medicines List was 84.7%. Patient care indicators had 6.47 minutes as the average consultation time, 160 seconds as the average dispensing time, 97.5% as medicines actually dispensed, 84.19% medicines adequately labelled and 76.67 had knowledge of correct doses. The availability of an EML was 100%. Key essential drugs availability in the clinic was determined to be 56% drugs during data collection. This study will help in understanding rational antifungal prescription practices and help in directing future studies. The findings of this study will assist the Kingdom of Eswatini to recognize the need to develop well established antifungal management protocols or/and programs.

Keywords: essential medicines list; rational drug use; WHO/INRUD core drug use indicators

1. Introduction

Eswatini, officially kingdom of Eswatini, previously known as the Kingdom of Swaziland, is a landlocked country bordered by Mozambique to its northeast and South Africa to its north, west and south. It covers a total are of 17,364 km^2 and it has a population of 1,062,000 which was estimated in 2017 [1]. Eswatini's administrative and judicial centre is Mbabane and the legislative centre is Lobamba [2]. The severity of fungal infections ranges from asymptomatic-mild mucocutaneous infections to potentially life-threatening systemic infections [3]. Fungal infections pose a serious threat to human health and life [4]. These fungal infections can be classified as supercritical, cutaneous and subcutaneous infection, as well as systemic fungal infections [5]. In recent years, there has been an increase in fungal infection and two major populations are more susceptible for acquiring invasive fungal infections [6]. The first population consists of individuals that live in endemic geographic location, for example infections such as Histoplasma caspsulatum var. capsulatum along the Mississippi River Valley, Coccidioides immitis in the southwest of the United States of America and Blastomyces dermatitidis in the central and southeastern states of America [7]. The second population consists of individuals with increased host susceptibility, who develop opportunistic infections, for example, severely

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ill individuals, hospitalized patient population who need care in specialized units and the use of invasive monitoring devices, parenteral nutrition, broad spectrum antibiotics and assisted ventilation. Additionally, the second population also comprises of immunocompromised patients due to newer technologies and people with primary immunodeficiences that are genetic disorders involving one or multiple components of the immune system. The World Health Organization (WHO) described rational drug use (RDU) as patients receiving the appropriate medications for best possible effect, in doses that meet their requirements within a short duration and at lowest cost possible [8]. On the other hand, irrational drug use is when one or more of these conditions is not met. Measurement of drug use in health facilities not only describes drug use patterns and prescription behavior but also helps in the identification of factors responsible for the practice of polypharmacy and the problems related with it [9]. Prescriptions are a legal document holding the prescriber and the dispensing pharmacist responsible for all the drugs that are prescribed and dispensed [10]. On the other hand, described a complete prescription as a verbal, written or electronic order for medication issued by a qualified prescriber which contains the core parts of prescription [10]. These parts include prescriber information (name, address, qualification, telephone number and practice number), patient information (full name, address, weight, age, allergy status), date, superscription (heading where the ”Rx” symbol is found), drug information (drugs name, quantities of active ingredient, dose and dosage form), subscription (specific directions for pharmacist), signatura (specific directions for patient) and prescriber signature. In addition, the presence of these core parts of a prescription and other data aims at a more rational use of drugs, minimizing drug-related problems and improving treatment outcomes. WHO and the international Network of Rational Use of Drugs (INRUD) have developed a set of drug prescribing indicators to be used as measures of prescribing performance in primary care. Assessment of drug use patterns using the WHO/INRUD core drug indicators has been successfully implemented in more than 30 developing countries. The WHO/INRUD core drug use indicators are reliable in measuring aspects of health provider behavior in primary healthcare facilities. These indicators provide information on prescribing performance concerning medicine use, prescribing patterns and important aspects of patient care. In addition, the core drug use indicators measure performance in three related areas of prescribing practices, patient care and facility specific factors [11].

Dermatological diseases are prevalent globally and constitute a quarter of cases in the practice of a physician [12]. Fungal diseases kill more than 1.5 million and affect over a billion people. It is estimated that nearly a billion people have skin, nail and hair fungal infections, 10’s of millions mucosal candidiasis and more than 150 million people have serious fungal infections. Recent global estimates found 3,000,000 cases of chronic pulmonary aspergillosis, ~223,100 cases of cryptococcal meningitis complicating HIV/AIDS, ~700,000 cases of invasive candidiasis, ~500,000 cases of Pneumocytis jirovecii pneumonia, ~250,000 cases of invasive aspergillosis, ~100,000 cases of disseminated histoplasmosis, over 10,000,000 cases of fungal asthma and ~1,000,000 cases of fungi keratitis occur every year [13]. In the United States of America 25,000 cases of coccidioimycosis and 25,000 cases of histoplasmosis are diagnosed annually [14]. Paracoccoidiodomycosis caused by a dimorphic fungus Paracoccoidioides brasiliensis, is estimated to cause about 4000 life threatening infections in Brazil, which carries a mortality rate of 5-27% [15]. There are over 8000 cases of Penicillosis due to Penicilium marneffei in Southeast Asia [16].

In France, it is predicted that there is high prevalence of severe asthma with fungal sensitization episodes (189 cases/100,000 adults per year), allergic bronchopulmonary aspergillosis (145 cases/100,000 adults per year), and chronic pulmonary aspergillosis (5.24 cases/100,000 adults per year) [17]. Every year the estimated incidence of invasive aspergillosis is 1.8 cases/100,000 adults per year based on classical high risk factors. Estimates for invasive mucormycosis (zygomycosis), pneumocystosis and cryptococcosis are 0.12 cases/100,000 adults per year, 1 case/100,000 adults per year and 0.2 cases/100,000 adults per year respectively [18]. More than 10,000 cases of invasive candidiasis are estimated annually. In Spain, around 8.1 million people suffer a fungal infection every year which are mostly skin or mucosal infections causing no deaths [19]. Candidaemia is more common in Spain than in other European countries and has risen by 1.88- fold in frequency in the last decade (8.1 cases of 100,000 people). There good estimates available of invasive aspergillosis (2.75 case of 100,000 people) and mucormycosis (0.04 cases of 100,000 people). Fungal infections with a high mortality such as invasive aspergillosis, candidaemia, Pneumocystis pneumonia and mucormycosis are not numerous in Spain but affect people with severe underlying diseases and are therefore linked to poor outcomes. Cryptococcal meningitis is the leading cause of adult meningitis in sub-Saharan Africa, and contributes up to 20% of AIDS-related mortality in low-income and middle-income countries annually [20]. Only a few classes of antifungal drugs are available to treat this infection, therefore the emergence of resistance to single drug

classes and now multidrug resistance greatly affects patient management. The unavailability and local costs of flucytosine and amphotericin B were documented in 10 countries with a high burden of cryptococcal meningitis in Africa. Neither drug was available in Ethiopia, Democratic Republic of Congo, Guinea, Cameroon or Tanzania. Flucytosine was also not available in Eswatini, South Africa, Uganda, Kenya or Sudan [21].

Inappropriate use of antifungal agents is implicated in the development of antifungal resistance and can lead to adverse outcomes like persistent infections, unnecessary exposure and increased cost [22]. However, data is limited on antifungal consumption in high-risk areas. This problem is of concern to developing countries including the kingdom of Eswatini because of the absence of well-established antifungal management protocols and/or programs. In addition, there is also limited data on the incidence and/or prevalence of inappropriate use of antifungals and the risks associated with it in these countries. In the last four years, the Leading International Fungal Education (LIFE) portal has facilitated the estimation of the burden of serious fungal infections country by country [23]. However, a precise estimate of global prevalence and incidence for each fungal infection remains unknown and data are minimal in most countries, especially developing countries. Based on a map showing completed country estimates of fungal diseases, Eswatini had no available data. Knowledge about the global incidence of fungal infections in countries like Eswatini has been impaired by lack of regular national surveillance systems, no obligatory reporting of fungal diseases, poor clinician suspicion outside specialized units, poor diagnostic test performance (especially for culture) and few well-designed published studies [23]. Hence, this study was carried out in the Kingdom of Eswatini because of the absence of well-established antifungal management protocols and/or programs and limited data on the incidence and/or prevalence of inappropriate use of antifungals and the risks associated with it. The study was also carried out to influence rational drug use because of the likelihood of adverse outcomes like persistent infections, unnecessary exposure and increased cost caused by inappropriate use of antifungal medications.

Over 80% of patients could be saved from dying with universal availability of fungal diagnostics and potent antifungal agents, based on well documented treatment response rates [23]. However, in developing countries like Eswatini, the early recognition and management of serious fungal infections is always a challenge, due to limited resources as antifungal treatment can be expensive and/or toxic. Other factors affecting better outcome include lack of patient compliance with long-term treatment, drug-drug interactions, drug-food interactions, limited clinical experience of excellent care in many settings and co-morbidities reducing the likelihood of survival and cure. In Eswatini, there are no reports on the utilization pattern of the use of antifungal agents. Most case reports on specific types of fungal infections and their management are not published. To date, no study from Eswatini has reported rational use of antifungal medications at the clinic in Mbabane. Therefore, it was of vital importance that a study be carried out so as to assess the rational use of antifungal drugs and administration to patients in the clinic in Mbabane, Eswatini.

The surveillance of antimicrobial use in hospitals is an important means of observing prescribing trends, linking results with antimicrobial resistance patterns and identifying areas for improvement in safe and effective prescribing [24]. It is therefore anticipated that the study might benefit the following population: The findings of this study might assist the nation of Eswatini to recognize the need to develop well established antifungal management protocols and/or programs. Eswatini might also develop well documented treatment response rates to record data on the incidence and/or prevalence of inappropriate use of antifungals and the risks associated with it. It could also lead to regular national surveillance systems, obligatory reporting of fungal infections and well-designed published studies. The researcher anticipates that the study might help health care workers to be adequately trained on appropriate prescribing and dispensing of antifungal medications which could reduce the development of antifungal resistance as well as adverse outcomes like persistent infections, unnecessary exposure and increased cost. The findings of this study might promote rational drug use of antifungals which will benefit the society by minimizing drug-related problems and improving treatment outcomes of patients.

The purpose of this study is to assess the rational use of antifungal medications by using WHO/INRUD core drug use indicators at a clinic in Mbabane, Eswatini.

2. Materials and Methods

Virtual To assess prescriber's indicators of antifungal prescriptions in the clinic and to assess completeness of antifungal prescriptions written by prescribers in the facility, the study design included a retrospective, cross sectional descriptive study to assess prescribing indicators and completeness of antifungal prescriptions. To

investigate patient care indicators of antifungal prescriptions in the clinic and to evaluate facility specific indicators of antifungal prescriptions in the clinic, A prospective, cross sectional study was used for patient care and facility specific indicators. A descriptive research is used to obtain information concerning the current status of a phenomenon and to describe what exists with respect to variables. A cross sectional research design measures differences between or among a variety of people, subjects or phenomena [16 Barratt & Kirwam, 2009).

The study was conducted to assess the WHO/INRUD core drug indicators at a clinic in Mbabane, Eswatini. Mbabane is the capital city of the kingdom of Eswatini in the Hhohho region. Located in the Highveld, it has an average height of 1243 meters. Mbabane is surrounded by the Mdzimba mountain and is a gateway to Sibebe Rock. Regardless of the fact that it is regarded as a medium sized town by western standards with a population of about 95,000, it is estimated as Eswatini's largest city.

The government of Eswatini listed the following health facilities in Mbabane, Mbabane Government hospital, Mbabane public health unit, Mbabane City Council clinic, Mbabane clinic, SOS clinic/ SOS Children's Village clinic, Mahwalala Red Cross clinic, Family Life Association clinic and Baylor C.O.E clinic. For ethical reasons the identity of the clinic was not revealed. The map of Eswatini showing Mbabane is shown in Fig. 1.

Fig. 1. The map of Eswatini showing Mbabane.

The study population was all the antifungal prescriptions between 1st January 2018 and 31st December 2018 (one year) and data outside this period was excluded. Outpatients in July 2019 (which was the actual time the research was conducted) and one Pharmacy personnel at the clinic in Mbabane were included. A total of 168 prescriptions were randomly selected and used by random sampling method. Only 168 antifungal prescriptions instead of WHO recommended 600 prescriptions were accessible in the Electronic Medical Records through the Client Management Information System (CMIS) version 2.0. A total of 30 outpatients were randomly sampled. One pharmacy personnel was interviewed.

The blank examples of prescribing indicators form, patient care form and facility summary form were used to collect the required variables using WHO/INRUD core drug use indicators. Antifungal prescriptions were observed for completeness, questionnaires were used to collect data on patient care indicators and facility specific indicators along with observation.

Antifungal prescriptions of patients attending the clinic in Mbabane for the period from 1st January 2018 to 31st December 2018 were collected. A total of 168 prescriptions were sampled using random sampling to minimize the bias. Thirty patients attending the clinic in Mbabane for diagnosis and treatment of fungal infections were included in the cross sectional study. Patients selected in the study were of different age groups and they were observed and interviewed using a questionnaire. Patients that were included in the study were those that were willing to participate and that had signed the informed consent. One pharmacy personnel from the clinic in Mbabane was interviewed using a questionnaire. This personnel was observed. The collected data was presented using tables and graphs, and descriptive statistics such as percentages were calculated. Data entry and analysis was conducted using SPSS (Statistical Package for Social Sciences) for windows version 20.

The research proposal was presented at the Eswatini Medical Christian University (EMCU) at a defense meeting with the Pharmacy Department on the 13/14th November 2018 for approval. Upon approval, the proposal was submitted to EMCU Research and Ethics Committee. After approval by the EMCU Research and Ethics committee, it was then submitted to the Eswatini Ministry of Health Research and Ethics Committee

(National Health Research Review Board) for final ethical clearance. Once approved, a letter was written by the HOD of the Pharmacy department at EMCU, which was presented to the Senior Nurse of the clinic in Mbabane to obtain permission to collect data for the study. Permission was then granted and the research began.

A consent form for participation in the study was given to each participant to fill in. This was used to inform the participants about the study and their participation was voluntary. Only participants that had signed the consent form participated in the study. Each respondent was assured that the information provided by him/her would remain confidential to protect the participants' privacy. The gathered information was only assessable to the researcher and the supervisor. The participants were asked not to use their names. Codes were used instead. For ethical reasons, the identity of the health care facility in which the study was carried out was not revealed. It is a public clinic situated in the Hhohho region, in the capital city of Eswatini. Therefore, the results might not be generizable to the whole country and it is possible that results from other health facilities in the country might be different. The results of this study might not reveal reasons that lead to irrational use of antifungals in Eswatini and further studies could be required to reveal the reasons. In addition, the clinic provides health care services to a population of about 13 000. The clinic uses Electronic Medical Records through the Client Management Information System (CMIS) version 2.0. In this system only about 1200 prescriptions between 1st January 2018 and 31st December 2018 were accessible. More than 70% of these patients were on antiretroviral therapy (ART) only. Thus, only 168 prescriptions were antifungal prescription which did not meet the recommended and anticipated 600 prescriptions.

3. Results and Discussion

Table 1 and Fig. 2 depicted prescription information on patient information. The completeness of individual parameters of patients' information was shown. With regards to the name and address, age and sex of the patients, 100% were filled which was within the recommended standards of WHO (100%). On the other hand, the weight and allergy status of the patient did not comply with the standards of WHO (100%) that recommend that an ideal prescription should have all the patient information (name, address, age, weight, sex, allergy status) to be regarded as complete. The weight of the patient was mentioned on 91.1% of antifungal prescriptions. In the 8.9% of prescriptions without the weight of the patient, improper dosing can be a result and difficulties in dosage individualization. Patients' can be under dosed which increases the cost of treatment and leads to persistent fungal infections. On the other hand, some patients can be over dosed which can cause serious adverse effects. An interesting finding is that the allergy status was mentioned only on 3.6% of antifungal prescriptions which was very low when compared to the WHO standards of 100%. The lack of information on patients' allergy status may give rise to adverse drug events which may have severe consequences to patients. This problem may also further increase the cost of treatment for these patients and lead to unnecessary complications that could have been avoided if the allergy status of the patient were known. For example, a common adverse effect of griseofulvin is hepatotoxicity.

Among 285 prescriptions analyzed, most of the parameters(name, gender, age and date of consultation) were filled in more than 90% of the prescriptions except the address, body weight, and body mass index of the patient [25]. The demographic characters such as name, gender, age and date were present in 97.9%, 93.3%, 90.9% and 95%, respectively. However, the weight was only mentioned on 8.4% of prescriptions and address of the patient was mentioned only on 1.8%.

Table 1. Patient information.

		N	N%
Name and address	Present	168	100.0%
	Absent	0	0.0%
Age	Present	168	100.0%
	Absent	0	0.0%
Weight	Present	153	91.1%
	Absent	15	8.9%
Sex	Present	168	100.0%
	Absent	0	0.0%
Allergy status	Present	6	3.6%
	Absent	162	96.4%

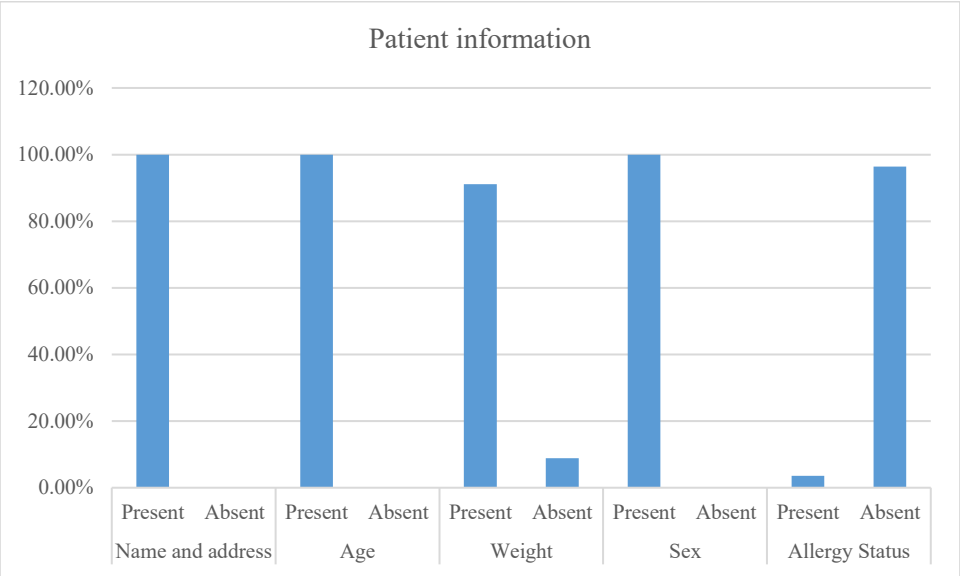

Fig. 2. Patient information.

Even Table 2 and Fig. 3 depicted prescribers' information. The name and the address of the prescribing physician were present in 98.2% of the antifungal prescriptions which was almost as per the recommended optimal level of WHO (100%). The clinic used computerized physician order entry system which resulted in all of the prescriptions lacking the department, registration number and signature of the prescribing physician (0.00%) which did not meet the recommended values of WHO as a complete prescription should have the department, registration number and signature (100%). All the 285 prescriptions were written with the name and address of the prescribing physician (100%). 98.6% of prescriptions contained contact number and specialty (department) of the physician that had prescribed. 98.6% of the prescriptions were signed by the physician.

Table 2. Prescribers information.

		N	N%
Name and address	Present	165	98.2%
	Absent	3	1.8%
Department	Present	0	0.0%
	Absent	168	100.0%
Registration number	Present	0	0.0%
	Absent	168	100.0%
Signature	Present	0	0.0%
	Absent	168	100.0%

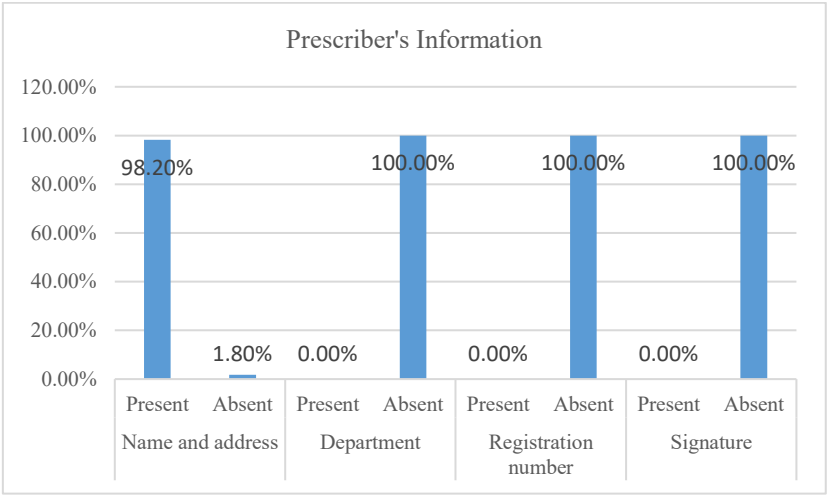

Fig. 3. Prescribers information.

Table 3 and Fig. 4 depicted Prescription details. It was found that most of the prescriptions contained the diagnosis (96.4%) which lacked 3.6% to be within the WHO standards. All the prescriptions were properly written with the drug name, drug strength, dosage form and route of administration, frequency and the duration (100%) and thus, the prescription met the recommended WHO/INRUD standards with regards to these parameters. However, all of the prescriptions lacked directions for the usage of the antifungal drugs (0%) which is extremely low when compared to 100% recommended by WHO. On the other hand, all of their collected prescriptions were properly written with the frequency of administration [25]. There were a few prescriptions that were missed with the strength (2.8%) and dosage form of the drugs (6.3%). In addition to that, most of the prescriptions were lacking with instructions for the usage of the drugs (94%) and route of administration of drug (94%).

Table 3. Prescription details.

		N	N%
Diagnosis	Present	162	96.4%
	Absent	6	3.6%
Drug name	Present	168	100.0%
	Absent	0	0.0%
Drug strength	Present	168	100.0%
	Absent	0	0.0%
Dosage form and route of admin	Present	168	100.0%
	Absent	0	0.0%
Frequency	Present	168	100.0%
	Absent	0	0.0%
Duration	Present	168	100.0%
	Absent	0	0.0%
Directions	Present	0	0.0%
	Absent	168	100.0%

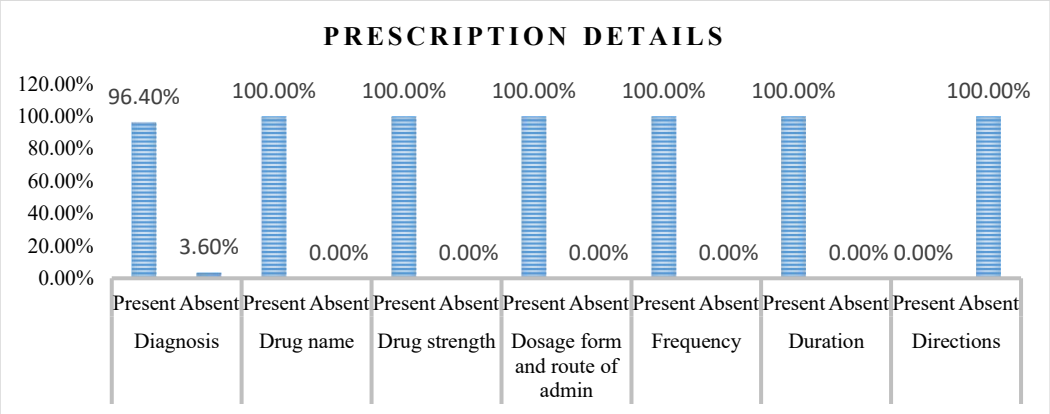

Fig. 4. Prescription details.

Tables 4 and 5, and Fig. 5 depict Patient care indicators. It was found that the average consultation time was only 6.47 (SD=2.662) minutes which is shorter than the optimal consultation time proposed by WHO/INRUD which is ≥10 minutes. The consultation time found (6.47 minutes) is too short to conduct a complete patient evaluation and prescribe therapy. Thus, the short consultation time reported could have been because of a low number of physicians. The clinic only had nurses (6) that were responsible to prescribe and dispense. There was no pharmacist or pharmacy technician. In a study conducted in primary healthcare centers in Alexandria, Egypt, the average consultation time was only 7.1 minutes which is a short consultation time based on the optimal values of WHO/INRUD [26]. In another study conducted in Pakistan, the average consultation time was 1.2 minutes which is extremely shorter than the optimal consultation time proposed by WHO/INRUD [27]. The average dispensing time reported in this study was 160 (SD=89.597) seconds. This is acceptable as compared with the optimal dispensing time recommended by WHO/INRUD which is ≥90 seconds. Thus, the average dispensing time was sufficient to explain dosage regimen, adverse effects and all

precautions of antifungal medicines. In a public hospital in Ethiopia, the average dispensing time was 3.66 minutes (219.6 seconds) which is sufficient time as recommended by WHO/INRUD [28].

Table 4. Patient information. 'a' denotes multiple modes exist. The smallest value is shown.

		Consultation time (mins)	Dispensing time (secs)	Number of drugs prescribed	Number of drugs dispensed	Number adequately labelled
N	**Valid**	30	30	30	30	30
	Missing	0	0	0	0	0
Mean		6.47	160.00	3.57	3.47	3.00
Mode		5	60[a]	4	3	2
Standard Deviation		2.662	89.597	1.478	1.479	1.438

Table 5. Patient care information in percentages.

		Percentage of dispensed drugs	Percentage of correctly labelled drugs
N	**Valid**	30	30
	Missing	0	0
Mean		97.50%	84.19%
Mode		100%	100%
Std. Deviation		7.628%	16.745%
Range		25%	50%
Minimum		75%	50%
Maximum		100%	100%

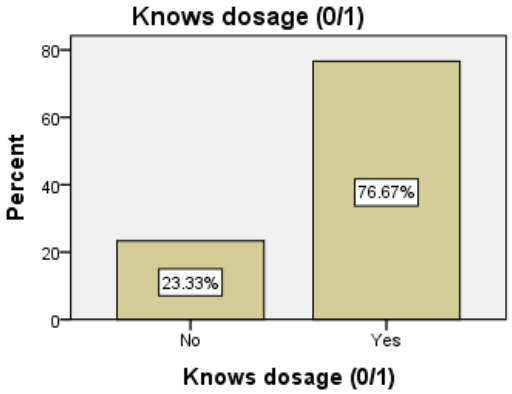

Fig. 5. The knowledge of dosage.

Tables 6 and 7 illustrated the prescribing indicators. In the present study, the average number of drugs per prescription was 3.3 and the most common number was 3 drugs per prescription while 8 drugs in one prescription was the highest, 1 drug was the minimum. An average of 3.3 drugs per encounter is way beyond WHO/INRUD optimal value of 1.6-1.8, it is actually double that value. In study conducted in Bahawal Victoria Hospital, Pakistan, using the WHO INRUD prescribing indicators found out that the average drugs per encounter was 2.3 which is still well above the optimal value of 1.6-1.8 but it was lower than results from this study [27]. In a study conducted to evaluate consequences of polypharmacy in elderly, it was stated that prescribing many drugs in one prescription or more than medically necessary is known as polypharmacy. Polypharmacy increases the healthcare costs, increases risks of drug-drug interactions and it promotes medication non-adherence [29]. Thus, the high number drugs per encounter in this study and the mentioned study is irrational drug use. For simple and universal communication among healthcare workers, WHO recommended the use of generic names of drugs instead of brand names [30]. In this study 87.7% (SD=18.3%) of the drugs were prescribed by their generic names, which is below the optimal value set by WHO which is 100%. When comparing to other studies this value is lower as in Timor-Leste it was 92% [31] and in Ethiopia it was 98.7% [32] but these studies report values that are almost similar with the WHO/INRUD standard derived to serve as ideal (100%). Findings of this study was higher than the one that was conducted in Pakistan, 83.1% [30]. The main objective of this study was to assess the rational drug use of antifungals. However, it is common

that health care workers mix antibiotics and antifungals, yet antibiotics are ineffective against fungal infections. An antibiotic can be prescribed together with an antifungal in case of a secondary bacterial infection. In this study, the mean percentage of antibiotics prescribed was 6.24% (SD=10.4%). This number is relatively low as compared to the standards of 20.00-26.8% set by WHO/INRUD meaning that antibiotics are rationally used at the clinic in Mbabane where the study was conducted. In other African countries the numbers of encounters with an antibiotic prescribed are higher. In a study conducted in Botswana, antibiotic prescribing was 42.7% with 14.7%, 5.9% and 1.3% of prescriptions having two, three and four antibiotics, respectively [33]. On the other hand, in a study conducted in two provinces in South Africa antibiotic prescribing was 68.1% in public hospitals [34]. Unnecessary antibiotic prescribing is a leading cause for ADRs and leads to more frequent hospital admissions [35]. Currently, the problem of antibiotic use is receiving global attention as a result of increasing antimicrobial resistance. There are multiple routes of administration of drugs but the most common being the oral route. It is not only common but it is also economic and requires no specialized skills or special equipment's for administration. Thus, making it a preferred route of administration over injectables. In this study, the percent encounters with an injection prescribed was 0.45% which is below the WHO/INRUD optimal value of 13.4 -24.1%. In Eswatini, clinics usually do not keep injectables in their stock which can explain this value. Also the fact that most of the antifungals that are available in Eswatini are of the oral dosage form. The findings of this study are incomparable with other studies. The values in other studies is way too high like the one in Pakistan whereby the value was 98% which also doesn't meet the standards set by WHO/INRUD [30]. With regards to prescribed drugs being on the EML, the findings in this study are comparable with other studies as 84.7% (SD=26.4%) average prescribed drugs were the on EML. In Lao's People Republic it was 86.2% [36]. Rational drug use involves prescribing drugs from EML issued by WHO since these drugs are older and are time tested and lower at cost than the branded originator drugs [37]. The WHO/INRUD optimal values regarding percent medicines prescribed from EML is 100% thus in this study the findings fell short.

Table 6. Prescribing indicators.

		Number of drugs prescribed	Number of generics	Number of antibiotics	Number of injections	Number on EDL
N	**Valid**	168	168	168	168	168
	Missing	0	0	0	0	0
Mean		3.30	2.91	0.29	0.02	2.89
Mode		3	3	0	0	2
Standard Deviation		1.562	1.555	0.491	0.133	1.582

Table 7. Prescribing indicators in percentages.

		Percentage of generic	Percentage of antibiotics	Percentage of drugs on EML	Percentage of injections
N	**Valid**	168	168	168	168
	Missing	0	0	0	0
Mean		87.77%	6.24%	84.73%	0.45%
Mode		100%	0%	100%	0%
Std. Deviation		18.661%	10.885%	26.421%	3.321%
Range		67%	40%	100%	25%
Minimum		33%	0%	0%	0%
Maximum		100%	40%	100%	25%

Fungal infections are on the rise worldwide and Africa is worse due to the HIV/AIDS pandemic resulting in immunocompromised patients. Antifungal resistance has been reported and it is on the rise, this suggests that antifungal agents should be used rationally [3]. Table 8 and Fig. 6 show the age of patients and gender of patients, respectively. In the sample of 168 participants being treated for fungal infections, the average age of patients was 21 years and the youngest was 7 years old. On the other hand, in a study conducted in Oman, 244 patients were included and the average age of patients was 37 years [38]. In terms of gender it was almost 50-50 with females being 49.4 % and males being 50.6% which is comparable with the study in Oman that reported 56.1 % males and 43.9% females. These values were different than those reported [39] who found out that there was statistically significant correlation between yeast infection and gender, females being affected more.

Table 8. The age of patients. 'a' denotes multiple modes exist. The smallest value is shown.

N	**Valid**	168
	Missing	0
Mean		21.65
Mode		7[a]
Standard Deviation		16.722

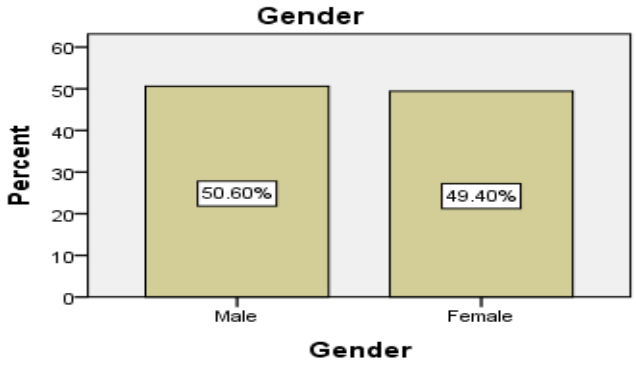

Fig. 6. The gender of patient

Fig. 7 depicts the fungal condition of patients. The most prevalent fungal condition among the sample was Tinea corporis (57.74%) which is also known as ringworm, a superficial fungal infection. These findings are in line with a report released by CDC in 2011, the most prevalent fungal infection in the US was tinea corporis. Fig. 8 illustrated the most common type of fungal infection being dermophytic infections (86.31%) compared to opportunistic infections (13.69%). Opportunistic fungal infections mainly occur in immunocompromised patients [40], which is supported by [41], 58 to 81% of AIDS patients at some time contract fungal infection. Patients with AIDS are immunocompromised which why they are at high risk of contracting opportunistic fungal infections. However, in this sample the number is very low due to safety measures introduced in the National Guidelines for the management of HIV/AIDS, as well as, HAART which reduces viral load of patients and increases immunity of the patient. Thus, in Eswatini the number of immunocompromised patients can be said to be greatly decreasing. Most of the fungal infections are dermophytic, mainly ringworms and yeast infections. On the other hand, Fig. 4.42 shows other fungal infections other than tinea corporis. In this study the findings on fungal conditions of patients showed oral candidiasis as the second most prevalent with 15.48% while fungal dermatitis was 14.88%. In addition, vaginal candidiasis was 4.76%. The least prevalent fungal condition was genital candidiasis as it was 4.76%. In a study conducted in Oman, superficial fungal infections (tinea pedis, sporotrichosis, vulvovaginal candidiasis) were the common form of fungal infections [22].

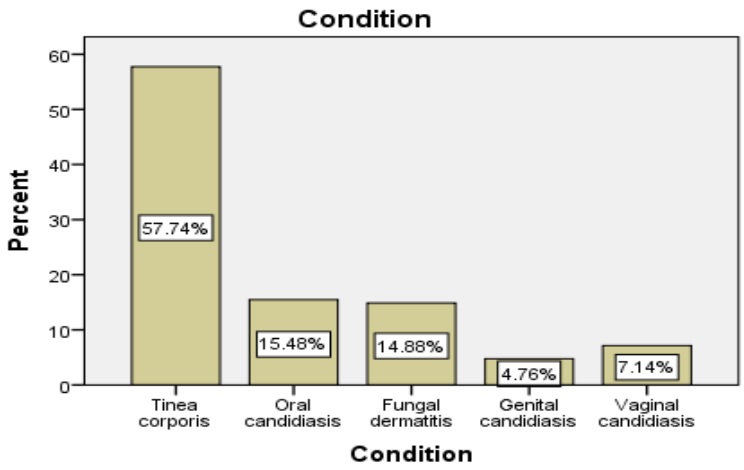

Fig. 7. The condition of patients.

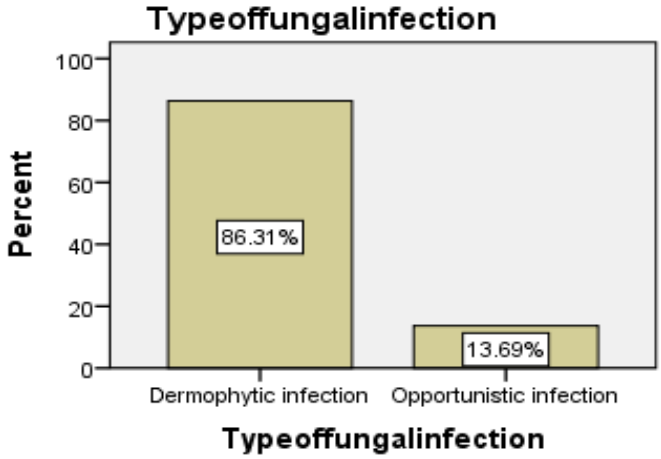

Fig. 8. The type of fungal infection.

Fig. 9 depicts the percent of each antifungal medication used. Benzoic acid is one of the most commonly used antifungal agent in the clinic in Mbabane (27.98%) followed by Griseofulvin (16.07%). The least use antifungal medication was fluconazole (2.38%) which is a very costly antifungal drug that was rarely prescribed at the clinic where the research was conducted. The activity of benzoic acid and its ester have a reduced activity against Candida albicans, common causative agent of fungal infections [42]. The common use of benzoic acid in this present study can be explained by the fact that the most common type of fungal infection was ringworm, a superficial infection, hence benzoic acid ointment can be easily used.

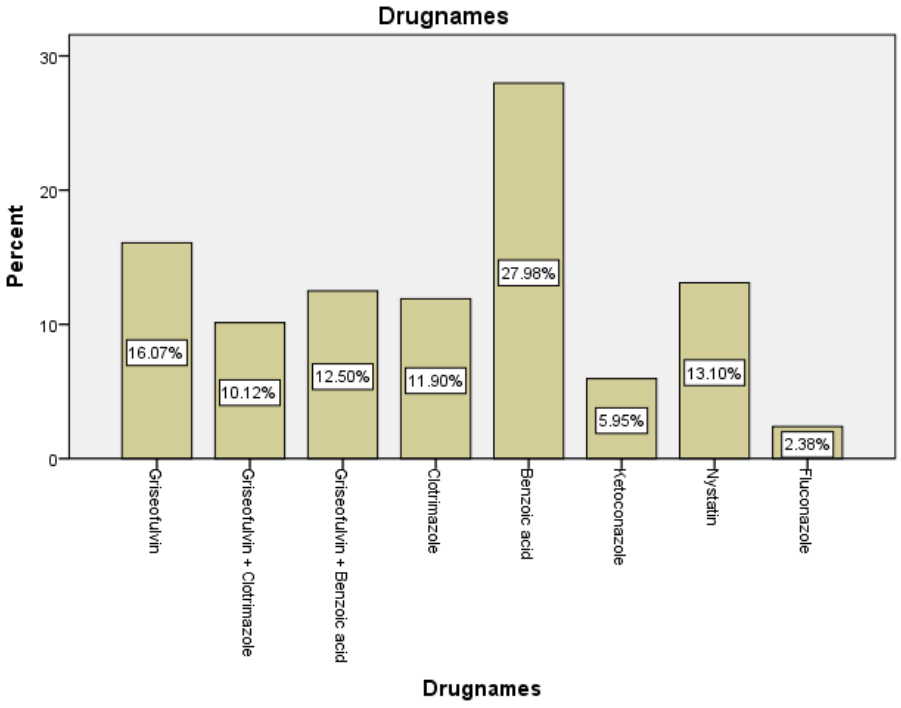

Fig. 9. The name of the antifungal medication.

Looking at Table 9, which shows the condition against the antifungal drug used, most of the drugs were rationally used, nystatin (22) was only prescribed for patients with oral candidiasis as per the STG. Griseofulvin is indicated to be used in tinea corporis as stipulated in the STG. Thus, in this study griseofulvin was used either alone (7) or in combination with clotrimazole cream (17) or benzoic acid (21). Ketoconazole is also indicated for use in tinea corporis as per the STG. Thus, the clinic in Mbabane prescribed the right antifungal medication for the right condition.

Table 9. Antifungal drug names versus the condition.

	Condition					
	Tinea corporis	**Oral candidiasis**	**Fungal dermatitis**	**Genital candidiasis**	**Vaginal candidiasis**	**Total**
Griseofulvin	7	0	12	8	0	27
Griseofulvin + Clotrimazole	17	0	0	0	0	17
Griseofulvin + Benzoic acid	21	0	0	0	0	21
Clotrimazole	8	0	0	0	12	20
Benzoic acid	44	0	3	0	0	47
Ketoconazole	0	0	10	0	0	10
Nystatin	0	22	0	0	0	22
Fluconazole	0	4	0	0	0	4
Total	97	26	25	8	12	168

Tables 10-12 depicts the gender versus the corresponding condition. More males (50) had tinea corporis than females (47) whereas equal numbers of males and females had oral candidiasis (13). Only 12 females had vaginal candidiasis. This showed that most fungal infections were predominant in both genders expect for vaginal candidiasis in females. In addition the dosage forms for the different prescribed drugs were correct. Pessaries were only given to female patients with vaginal candidiasis. Drops, gels and suspension were only used on patients suffering from oral candidiasis. WHO defines rational drug use as "patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements and at the lowest cost to them." Administering a tablet or drops or a gel to a patient suffering from vaginal candidiasis would increase the cost of therapy and it would not meet the clinical requirements of that patient hence that would be irrational drug use. In this study, that is not the case, all the standards of WHO's definition of rational drug use are meet. With regards to the duration, Griseofulvin is usually taken for 2 to 4 weeks for skin conditions, 4 to 6 weeks for scalp and hair conditions, 4 to 8 weeks for foot infection, and 3 to 4 months for toenail infections. In this study there was one participant that received Griseofulvin for 5 days, which is irrational drug use. It can result in resistant fungal strains developing. In Table 13 showed that griseofulvin was prescribed mostly for 2 weeks (15) and 4 weeks (11) as it was mostly prescribed to treat tinea corporis. Fluconazole was prescribed for a duration of 2 weeks in the 4 patients that received it. Pfizer recommends that fluconazole should be used for several days, up to two weeks thus it was rationally prescribed. The STG/EML provides little information on the appropriate use of antifungals thus it is difficult to compare the results to standards in Eswatini. Thus, it is recommended that the kingdom of Eswatini develop well established antifungal management guidelines to reduce the burden of serious fungal infections.

Table 10. The gender of patients versus the condition.

		Condition					
		Tinea corporis	**Oral candidiasis**	**Fungal dermatitis**	**Genital candidiasis**	**Vaginal candidiasis**	**Total**
Gender	**Male**	50	13	11	8	0	82
	Female	47	13	14	0	12	86
Total		97	26	25	8	12	168

Table 11. The form and condition.

		Condition					
		Tinea corporis	Oral candidiasis	Fungal dermatitis	Genital candidiasis	Vaginal candidiasis	Total
Form	Tablet	6	4	20	8	0	38
	Tablet + cream	18	0	0	0	0	18
	Tablet + ointment	24	0	0	0	0	24
	Suspension	0	13	0	0	0	13
	Gel	0	4	0	0	0	4
	Cream	8	0	2	0	3	13
	Pessary	0	0	0	0	9	9
	Ointment	41	0	3	0	0	44
	Drops	0	5	0	0	0	5
Total		97	26	25	8	12	168

Table 12. The duration of treatment versus the condition.

		Condition					
		Tinea corporis	Oral candidiasis	Fungal dermatitis	Genital candidiasis	Vaginal candidiasis	Total
Duration	1 week	35	16	3	0	11	65
	2 weeks	8	6	15	8	0	37
	3 weeks	32	0	7	0	0	39
	5 days	10	0	0	0	1	11
	8 weeks	0	4	0	0	0	4
	6 weeks	12	0	0	0	0	12
Total		97	26	25	8	12	168

Table 13. The antifungal drug name versus the duration.

		Duration						
		1 week	2 weeks	4 weeks	5 days	8 weeks	6 weeks	Total
Drug names	Griseofulvin	0	15	11	1	0	0	27
	Griseofulvin + Clotrimazole	0	0	14	0	0	3	17
	Griseofulvin + Benzoic acid	0	0	9	4	0	8	21
	Clotrimazole	19	0	0	1	0	0	20
	Benzoic acid	30	8	3	5	0	1	47
	Ketoconazole	0	8	2	0	0	0	10
	Nystatin	16	2	0	0	4	0	22
	Fluconazole	0	4	0	0	0	0	4
Total		65	37	39	11	4	12	168

Table 14 shows the availability of an Essential Medicines List or formulary. The pharmacy at the clinic in Mbabane where the study was conducted had an Essential Medicines List (100%). This is falls within the optimal value recommended by WHO/INRUD of 100%. In a study conducted in Egypt, the percentage of a copy of the EDL was 80% [26]. Presence of supportive reading material (formulary, drug list, treatment guideline) is vital for health professionals' continuous professional improvement and good patient outcomes [43]. WHO recommends adherence of physicians to the drugs listed in the EDL while prescribing medicati ons to ensure proper health care.

Fig. 10 depicted the percentage of key drugs in stock at the facility in Mbabane. In this current study, the average percentage of key drugs was 56%. The optimum standard set by WHO is 100% which the clinic did not meet. In a study conducted in Ethiopia to assess prescription completeness and drug use pattern in a hospital, key essential drugs availability was determined to be 82.5% [43]. Shortage of drug supply of essential drugs that treat common health problems is harmful to health status of patients. The findings versus WHO/INRUD optimal values are listed in Table 15.

Table 14. Facility specific indicators.

	Frequency	Percentage
Yes	1 formulary	100%

Table 15. The findings versus WHO/INRUD optimal values.

CORE DRUG USE INDICATORS	FINDINGS	OPTIMAL VALUES
PRESCRIBING INDICATORS		
Average number of drugs per patient encounter	3.30	1.6-1.8
Percent medicines prescribed by generic name	87.77%	100%
Percent encounters with an antibiotic prescribed	6.24%	20.00-26.8%
Percent encounters with an injection prescribed	0.45%	13.4-24.1%
Percent medicines prescribed from essential medicines list or formulary	84.73%	100%
PATIENT-CARE INDICATORS		
Average consultation time (minutes)	6.47 min	≥10 min
Average dispensing time (seconds)	160 sec	≥90 sec
Percent medicines actually dispensed	97.50%	100%
Percent medicines adequately labeled	84.19%	100%
Percent patients with knowledge of correct doses	76.67%	100%
FACILITY-SPECIFIC INDICATORS		
Availability of essential medicines list or formulary to practitioners	100%	100%
Percent key medicines available	56%	100%

The Based on the findings in this study, antifungal drugs were irrationally prescribed. The findings were below the optimal values recommended by WHO/INRUD. With regard to the prescribing indicators, all of the parameters were either below or above the optimal value stipulated by WHO/INRUD. On the other hand, patient care indicators did not conform to the WHO/INRUD standards except for the average dispensing time of 160 seconds which was within the standards of ≥90 seconds. The facility specific indicators met the standards set by WHO/INRUD as there was a copy of an EML (100%).

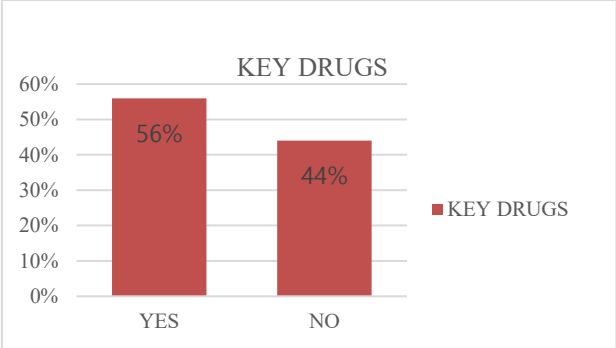

Fig. 10. The availability of key drugs.

With regards to the pattern of use of antifungals, the most prevalent fungal condition among the sample was Tinea corporis (57.74%) which was appropriately treated with griseofulvin and in some instances benzoic acid. The antifungal medications were prescribed for the right fungal conditions as per the STG and the durations were sufficient except for one patient that was prescribed griseofulvin for 5 days. In addition the dosage forms were also appropriate for treating the specific conditions. Due to limited data in the Hhohho region, the findings of this study cannot be generalizable to the entire kingdom of Eswatini. Thus, it is recommended that this study could help in directing future studies. Thus, the country could eventually develop well-established antifungal management protocols and/or programs. In the last four years, Eswatini along with other developing countries had minimal data and the prevalence and burden of serious fungal infections remained unknown. Ultimately, the kingdom of Eswatini could have data on serious fungal infections which is facilitated by LIFE portal and depicted in a map of the world as global fungal infection prevalence. Eswatini could also develop well documented treatment response rates in order to save people from dying by providing universal availability of fungal diagnostics and potent antifungal agents.

Another recommendation is for the Government of Eswatini to ensure that there are well trained pharmacists and pharmacy technicians in public clinics and hospitals as they are experts in drugs and dispensing. As well as highly skilled physicians to prescribe in these public clinics and hospitals.

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Conflicts of Interest: The author has no conflict of interest related to this study to disclosure.

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